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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/890,478	07/31/2001	Andrea Pizzariello		1759

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EXAMINER	
NOGUEROLA, ALEXANDER STEPHAN	
ART UNIT	PAPER NUMBER
1753	

DATE MAILED: 01/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/890,478	PIZZARIELLO ET AL.	
	Examiner	Art Unit	
	ALEX NOGUEROLA	1753	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 January 2005*.

2a)☒ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *14 and 15* is/are allowed.

6)☒ Claim(s) *1-7,9-13 and 16* is/are rejected.

7)☒ Claim(s) *8 and 17* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 July 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Objections and Rejections pending since the Office action of July 09, 2004

1. The objection to claim 14 is withdrawn.

2. All rejections under 35 U.S.C. 112, second paragraph, are withdrawn.

3. The rejections of claims 1-3, 5-7, 9-13, and 16 under 35 U.S.C. 102(b) as being anticipated by Kulys are withdrawn.

4. The rejections of claims 1-3, 5, 6, 10, 11, and 16 under 35 U.S.C. 102(b) as being anticipated by Nishizawa are withdrawn, but have been rewritten in light of Applicants' amendment.

5. The rejections of claims 1-3, 6-12, and 16 under 35 U.S.C. 102(b) as being anticipated by Castanon are withdrawn.

6. The rejection of claim 4 under 35 U.S.C. 103(a) as being obvious over Nishizawa is withdrawn, but has been rewritten in light of Applicants' amendment.

Response to Amendment

7. Applicants' amendment of January 10, 2005 ("Amendment") does not render the application allowable.

Response to Arguments

8. Applicant's arguments filed January 10, 2005 have been fully considered but they are not persuasive. Applicants argue

> ... the invention recited in Claim 1 is also novel with respect to Nishizawa et al. based on a contention that Claim 1 recites an ammeter but Nishizawa et al. does not disclose an ammeter. The Examiner indicated that an ammeter is implied by Figure 2 of Nishizawa but Applicants respectfully submit that Figure 2 does not imply the ammeter. Ammeters measure electrical current intensity - Amperes - flowing through a material and do not measure an electrical property of the material - conductivity. In contrast, the device which is implied by Figure 2 of Nishizawa measures an electrical property of the material, namely, conductivity based on a view that the Y axis of Figure 2 is identified by I_D - a unit of conductivity. As such, the device implied by Figure 2 is a conductometer and not an ammeter. Hence, Claim 1 is believed to be novel with respect to Nishizawa et al. *See page 8 of the Amendment.*

The examiner respectfully disagrees with Applicants view that Nishizawa does not disclose an ammeter. The circuit schematic in Figure 2 shows a symbol for an ammeter (the "A" in a circle); the caption for Figure 1 states that "I_D" represents current; the y-axis for Figure 5 shows that the units for "I_D" is "μA", that is microamperes, which Applicants themselves have stated is a measure of current (see the passage quoted above); and the Nishizawa states, "The

conductivity changes were detected by the increase in the **current (I_D)** between the two array ... [emphasis added]" (first column on page 2642).

Applicants also argue

> The biosensor as recited in Claim 1 operates in a different manner. In particular, the variation of pH changes the redox property of the compound, i.e., it modifies the equilibrium between the oxidized and reduced form of the compound. This modification of the equilibrium produces an electron current originating from the compound which is proportional to the analyte concentration and is monitored amperometrically. In sum, the compound as recited in Claim 1 does not merely receive and pass electrons but originates the electron current being measured. This novel and non-obvious approach results in biosensors which are not restricted to oxidisable analytes and improves sensitivity and linearity. . *See page 9 of the Amendment.*

Claims 1-3, 5, 6, and 10 are apparatus claims. Applicants arguments go to intended use. The asserted intended use is not reflected in the claimed language. Furthermore, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963).

Claims 11 and 16 are method claims however, claim 1 only broadly recites using the biosensor of claim 1 and claim 16 recites different fields of use, such as "human and veterinary diagnostics, industrial processes, ..." There is no requirement of operating the biosensor as set forth by Applicants.

Claim Rejections - 35 USC § 102

9. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

10. Claims 1-3, 5-7, 9-11, and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Nishizawa et al. ("Penicillin Sensor Based on a Microarray Electrode Coated with pH-Responsive Polypyrrole," *Anal. Chem.* 1992, 664, 2642-2644), hereafter "Nishizawa."

Addressing claim 1, Nishizawa teaches an amperometric biosensor system for the detection of analytes (Introduction) comprising

a) at least one biocatalyst (penicillase (Figure 1)) producing a pH change by its interaction with the analyte (first full paragraph in the second column on page 2643); the biocatalyst not belonging to a group of oxidoreductase enzymes;

b) at least one compound exhibiting different redox properties in its protonated and non-protonated forms (Figure 1 and the second full paragraph in the first column on page 2643) consisting of a heterocyclic compound containing between 3 to 30 carbon atoms and N heteroatom (see the structure for polypyrrole in the abstract of US 5,795,953));

c) a working electrode (Figure 1); and

d) a reference electrode (Figure 1);

e) the electrodes being connected through an ammeter (implied by Figure 2, which discloses measuring current).

Addressing claims 2, 3, and 5, Nishizawa discloses the enzyme penicillase (Figure 1)).

Addressing claim 6, in Nishizawa the pH-sensitive redox compound is polypyrrole, which is a polymer.

Addressing claim 7, Nishizawa discloses that a change in pH is reflected in a change in conductivity. See Figure 3. Indeed, "[w]e also found that the conductivity of the polypyrrole film is sensitive to pH of the solution.[8] This finding indicates that a polypyrrole-coated electrode serves as a pH-sensitive transducer for enzyme sensors [emphasis added]."

Addressing claim 9, in Nishizawa the working electrode is a platinum electrode. See Figure 1. and the first paragraph in the second column on page 2642.

Addressing claim 10, in Nishizawa the reference electrode is a calomel electrode (last full paragraphs in the second column on page 2642).

Addressing claim 11, Nishizawa discloses at least detecting penicillin (abstract).

Addressing claim 16, Nishizawa discloses measuring penicillin, which has use in at least the pharmaceutical industry.

Claim Rejections - 35 USC § 103

11. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

12. Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nishizawa et al. ("Penicillin Sensor Based on a Microarray Electrode Coated with pH-Responsive Polypyrrole," *Anal. Chem.* 1992, 664, 2642-2644), hereafter "Nishizawa."

Addressing claim 4, Nishizawa teaches an amperometric biosensor system for the detection of analytes (Introduction) comprising

a) at least one biocatalyst (penicillase (Figure 1)) producing a pH change by its interaction with the analyte (first full paragraph in the second column on page 2643); the biocatalyst not belonging to a group of oxidoreductase enzymes;

b) at least one compound exhibiting different redox properties in its protonated and non-protonated forms (Figure 1 and the second full paragraph in the first column on page 2643) consisting of a heterocyclic compound containing between 3 to 30 carbon atoms and N heteroatom (see the structure for polypyrrole in the abstract of US 5,795,953));

c) a working electrode (Figure 1); and

d) a reference electrode (Figure 1);

e) the electrodes being connected through an ammeter (implied by Figure 2, which discloses measuring current).

Although Nishizawa teaches penicillinase, Nishizawa does not specifically mention any of the enzymes listed in the Markush group of claim 4. However, it would have been obvious to one with ordinary skill in the art at the time of the invention to use other enzymes such as those listed in Applicant's claim 4, depending on the analyte or interest, because Nishizawa states, "[s]ince many enzymes bring about pH changes through their catalytic reactions, the principle proposed here will widely by applicable to the fabrication of enzyme-based microelectrochemical devices which detect biologically important substances" (second column on page 2644).

13. Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nishizawa et al. ("Penicillin Sensor Based on a Microarray Electrode Coated with pH-Responsive Polypyrrole," *Anal. Chem.* 1992, 664, 2642-2644), hereafter "Nishizawa," in view of Casta ón et al. ("Amperometric detection of ethanol with poly-(o-phenylenediamine)-modified enzyme electrodes," *Biosensors & Bioelectronics* vol. 12, no. 6, pp. 511-520), hereafter "Casta□ón."

Addressing claim 12, Nishizawa teaches an amperometric biosensor system for the detection of analytes (Introduction) comprising

a) at least one biocatalyst (penicillase (Figure 1)) producing a pH change by its interaction with the analyte (first full paragraph in the second column on page 2643); the biocatalyst not belonging to a group of oxidoreductase enzymes;

b) at least one compound exhibiting different redox properties in its protonated and non-protonated forms (Figure 1 and the second full paragraph in the first column on page

2643) consisting of a heterocyclic compound containing between 3 to 30 carbon atoms and N heteroatom (see the structure for polypyrrole in the abstract of US 5,795,953));

c) a working electrode (Figure 1); and

d) a reference electrode (Figure 1);

e) the electrodes being connected through an ammeter (implied by Figure 2, which discloses measuring current).

Nishizawa also discloses at least detecting penicillin (abstract); steps (a), (b), and (d) of claim 12 (first full paragraph in the first column on page 2643); and step (e) of claim 12 (Figure 5). As for step (c) of claim 12, measuring a background current, that is, running a "blank" sample to determine background noise, barring a contrary showing, this is just is a basic step in calibrating an analytical instrument, which would have been known to one with ordinary skill in that art of analytical chemistry instrumentation. Note that step (f) in claim 12 is optional. In any event, this step is just subtracting the background noise from the measured signal, which again is basic calibration procedure for analytical chemistry instrumentation. See for example Casta ón who discloses a biosensor and method of using a biosensor that is the same as that claimed except that the biocatalyst belongs to a group of oxidoreductase enzymes (see the rejections of claims 1, 11, and 12 based on Casta ón in the Office action of July 09, 2004). In particular, Casta ón discloses at least steps (a)-(e) (Analytical procedure on page 513 and Figure 7).

14. Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Nishizawa et al. ("Penicillin Sensor Based on a Microarray Electrode Coated with pH-Responsive Polypyrrole,"

Anal. Chem. 1992, 664, 2642-2644), hereafter "Nishizawa," in view of Kulys et al. ("Glucose biosensor based on the incorporation of Meldola Blue and glucose oxidase within carbon paste," *Analytica Chimica Acta* 288 (1994) 193-196), hereafter "Kulys."

Addressing claim 13, Nishizawa teaches an amperometric biosensor system for the detection of analytes (Introduction) comprising

a) at least one biocatalyst (penicillase (Figure 1)) producing a pH change by its interaction with the analyte (first full paragraph in the second column on page 2643); the biocatalyst not belonging to a group of oxidoreductase enzymes;

b) at least one compound exhibiting different redox properties in its protonated and non-protonated forms (Figure 1 and the second full paragraph in the first column on page 2643) consisting of a heterocyclic compound containing between 3 to 30 carbon atoms and N heteroatom (see the structure for polypyrrole in the abstract of US 5,795,953));

c) a working electrode (Figure 1); and

d) a reference electrode (Figure 1);

e) the electrodes being connected through an ammeter (implied by Figure 2, which discloses measuring current).

Nishizawa also discloses at least detecting penicillin (abstract); steps (a) and (c) of claim 13 (first full paragraph in the first column on page 2643); and step (d) of claim 13 (Figure 5). As for step (b) of claim 13, measuring a background current, that is, running a "blank" sample to determine background noise, barring a contrary showing, this is just is a basic step in calibrating an analytical instrument, which would have been known to one with ordinary skill in that art of analytical chemistry instrumentation. Note that step (e) in claim 12 is optional. In any

event, this step is just subtracting the background noise from the measured signal, which again is basic calibration procedure for analytical chemistry instrumentation. See for example Kulys who discloses a biosensor and method of using a biosensor that is the same as that claimed except that the biocatalyst belongs to a group of oxidoreductase enzymes (see the rejections of claims 1, 11, and 13 based on Kulys in the Office action of July 09, 2004). In particular, Kulys discloses at least steps (a)-(e) (last full paragraph in the second column on page 194; first paragraph of Results and Discussion on page 195; and Figures 1 and 2 of Kulys).

Allowable Subject Matter

15. Claims 14 and 15 are allowed.

16. Claims 8 and 17 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

17. The following is a statement of reasons for the indication of allowable subject matter:

a) Claim 8 requires the pH-sensitive redox compound to be selected from the specified Markush group. In Nishizawa the pH-sensitive redox compound is polypyrrole;

b) Claims 14 and 15 are allowable for the reasons set forth in the Office action of July 09, 2004; and

c) Claim 17 requires the pH indicator to be selected from the specified Markush group. In Nishizawa the pH-sensitive redox compound is polypyrrole.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ALEX NOGUEROLA whose telephone number is (571) 272-1343. The examiner can normally be reached on M-F 8:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, NAM NGUYEN can be reached on (571) 272-1342. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Alex Nogueroła
Primary Examiner
AU 1753
January 26, 2005